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| 10/783,259 | 02/20/2004 | Kenichiro Hasumi | 358690-00005-1 | 7322 |

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| EXAMINER | |
|---|---|
| HUMPHREY, LOUISE WANG ZHIYING | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/783,259 | HASUMI ET AL. | |
| | Examiner | Art Unit | |
| | LOUISE HUMPHREY | 1648 | |

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 3-15* is/are pending in the application.

4a) Of the above claim(s) *3-5,7,8 and 12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6 and 9-11* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is in response to the amendment filed 27 August 2008. Claim 2 has been cancelled. Claims 1 and 3-15 are pending. Claims 3-5, 7, 8 and 12-15 are drawn to a nonelected subject matter and hence are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 1, 6 and 9-11 are currently examined.

### *Claim Objections Necessitated by Amendment*

Claim 1 is objected to for failing to define the acronym "GM-CSF" at the first occurrence in the claims. Applicant may consider amending the claims to read --- granulocyte-macrophage colony-stimulating factor (GM-CSF)--- in step (b) of the claim for clarity. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This new ground of rejection is necessitated by the amendment to claim 1.

Regarding claim 1, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 6 and 9-11 are rejected for depending from an indefinite base claim.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1, 6 and 9-11 under 35 U.S.C. §103(a) as being obvious over Baxevanis *et al.* (1997) in view of Meidenbauer *et al.* (2000), Mengozzi *et al.* (2000) and Setaluri *et al.* (US 2002/0192727) is **withdrawn** in response to Applicants' amendment, which necessitates the following new grounds of rejection:

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kato *et al.* (2001, IDS 15 October 2007) in view of Mengozzi *et al.* (2001).

The instant claim is directed to a method of enhancing an immune response to an antigen in a mammal comprising:

(a) culturing naïve T cells with anti-CD3- and anti-CD28-coated beads to produce a lymphocyte conditioned media adjuvant;

(b) culturing monocytes with said lymphocyte conditioned media adjuvant in the absence of cytokines to produce immature dendritic cells;

(c) culturing said immature dendritic cells from step (b) with said lymphocyte conditioned media adjuvant in the presence of cytokines to produce mature dendritic cells; and

(d) administering said lymphocyte conditioned media adjuvant enriched with said mature dendritic cells in combination with a vaccine of said antigen to said mammal.

Kato *et al*. teach culturing naïve T cells with anti-CD3-coated plates to produce a lymphocyte conditioned media adjuvant referred to as "T cell conditioned medium" (TCCM) (page 942, left column, Preparation of TCCM), culturing monocytes in medium supplemented with lymphocyte conditioned medium or TCCM (page 942, Preparation of MCM) to produce immature dendritic cells (DC), culturing immature DC with T-cell-conditioned medium in the presence of cytokines to produce mature dendritic cells (Abstract, page 941, right column, first full paragraph, and page 942, Preparation of MCM), and using antigen-loaded DC to enhance immunity against cancer and infectious diseases (page 941, left column, INTRODUCTION). Kato *et al*. further disclose that the cell-free supernatants from anti-CD3-activated T cells [designated TCCM and termed lymphocyte conditioned media adjuvant in the instant claims] contain soluble factors that induce the terminal differentiation of immature DC to professional antigen presenting cells (page 947).

Kato *et al.* do not teach anti-CD3- and anti-CD28-coated beads.

Mengozzi *et al.* suggest using anti-CD3/anti-CD28-coated beads for *ex vivo* stimulation of T cells. Mengozzi *et al.* describe naïve T cells cultured with anti-CD3- and anti-CD28-coated beads. See first sentence in abstract. Mengozzi *et al.* explicitly suggest that CD3/CD28 stimulation (i.e., antibodies co-immobilized on beads) is one of the most powerful stimulants of cell activation and proliferation and results in maximal replication of naïve T cells. See page 11648, left column, last four lines, and right column, first full paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the T cell activation procedure of Kato *et al.* by replacing the anti-CD3-coated plates with anti-CD3 and anti-CD28-coated beads for co-stimulation of naïve T cells, as taught by Mengozzi *et al.* The skilled artisan would have been motivated to do so to more effectively activate naïve T cells so that the conditioned media would contain more soluble factors that facilitate dendritic cell maturation. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kato *et al.* (2001, IDS 15 October 2007) in view of Mengozzi *et al.* (2001) and Meidenbauer *et al.* (2000).

The instant invention is further limiting the antigen to prostate-specific antigen (PSA).

The disclosure of Kato *et al.* and Mengozzi *et al.* is set forth above. Kato *et al.* disclose cancer immunotherapy by administering DC with tumor-associated antigens, although Kato *et al.* do not specifically describe PSA.

Meidenbauer *et al.* disclose using administering a PSA-based vaccine in combination with an adjuvant (Abstract; page 89, 2nd column, to page 90).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the antigen of Kato *et al.* to PSA, as taught by Mengozzi *et al.*, in a formulation for cancer immunotherapy. The skilled artisan would have been motivated to do so to generate immune response for a therapy to treat prostate cancer. There would have been a reasonable expectation of success given that PSA elicits PSA-reactive T cells, as demonstrated by Meidenbauer *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kato *et al.* (2001, IDS 15 October 2007) in view of Mengozzi *et al.* (2001) and Setaluri *et al.* (US 2002/0192727).

The instant invention further limits the adjuvant dosage, administration route and schedule of the immunization method.

The disclosure of Kato *et al.* and Mengozzi *et al.* is set forth above. Kato *et al.* do not specifically describe any adjuvant dosage, administration route and schedule of the immunization method.

Setaluri *et al.* describe the dosage calculation and the administration of a tumor antigen hourly, daily, weekly, monthly, or yearly, by intramuscular or intravenous injection. See column 10, ¶90 and 92.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Kato *et al.* by adapting the dosage calculation, administration route and schedule taught by Setaluri *et al.* There would have been a reasonable expectation of success given the standard art-recognized dose and schedule for administration of an anti-tumor immunogen, as taught by Setraluri *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

Applicant's arguments with respect to claims 1, 6 and 9-11 have been considered but are moot in view of the new grounds of rejection as set forth above.

***Conclusion***

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call

800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

01 December 2008